## Update on Diagnosis and Treatment Subclinical Hyperthyroidism – CMDA December 2022 Presented by Michael McDermott MD University of Colorado Department of Endocrinology

CMDA colleagues. I became interested in this subject when I began to notice an epidemic of Methimazole prescribing in our facilities. Most seemed to be driven by routine TSH lab testing that came back with advice to diagnose subclinical hyperthyroidism if the TSH value was under 4. Here is a redacted sample from one of these patients:

A large regional lab had recently been noted to have erroneous information on their TSH reports: твн

TSH3		ulU/ml	0.450-5.330	Final			
In patients > 70 years, physiological TSH readings less than 4 uIU/mL may represent ?subclinical hyperthyroidism?. Although ?Normal? TSH readings are now defined as 4-6 uIU/mL in elderly patients, levels up to 10 uIU/mL may be physiological and do not necessarily need to be treated unless clinically indicated.							
тѕн	See Attachmen	t		Final			
Their lab director was co presentation). She took t that they agreed with this up to 4 may represent su discussion about subclini	ntacted and the information about TS his information to their committee that literature and they have subsequent bclinical hyperthyroidism. They now ical hyperthyroidism. Here is a redac	6H ranges in tt is respons tly removed just list the l ted example	the elderly (page 24 d ible for the lab reports the erroneous comme ower end of normal as from another patient f	of Dr McDermott's and she responded ents about the values 0.45 and no written from a recent test:			
TSH							

TSH3		ulU/ml	0.450-5.330	Final
TSH	See Attachment			Final

This prompted my contacting Dr McDermott at the University of Colorado about normal ranges of TSH in the elderly and what constituted subclinical hyperthyroidism. He affirmed that TSH values below 0.45 should be investigated for possible subclinical hyperthyroidism. This led to his agreeing to be our CMDA speaker this week on this condition.

On the right is slide 22 that the cut off for consideration of subclinical hyperthyroidism is a value of .45 (depending on which assay the specific lab is using it could be 0.4, 0.45 or 0.47 - he told me in a phone call). On this page he outlines the difference between a cutoff of 0.1 and a cutoff of 0.45. Below 0.1 strong consideration for treatment is recommended. Below 0.45 (and above 0.1) there needs to be a thoughtful consideration for treatment based on whether the patient has "symptoms" or risk factors. Symptom evaluation in an elderly and often demented patient is often fraught with hazard. Many articles recommend a wait and watch scenario if



the TSH is between 0.1 and .45 unless the risk factor consideration pushes you to treatment (my opinion from reading many articles recently when researching this subject).

Slide (24) below shows how the TSH distribution changes with age. The point of this slide is that **at the low end on the left the suppressed TSH guidance of using 0.45 doesn't change significantly with age.** The upper end does go up with age: thus you can take more of a wait and watch if the TSH is in the 6-8 or 6-10 range before starting therapy (different articles have differing advice). Note that the 4.0 value from the erroneous lab reports would have included approximately 75-80% of the patients depending on age interval.



**Fig. 1.** Shift in TSH distribution to higher concentrations with age. Data from NHANES III (NH3) and NHANES 1999–2002 (NH 99\_02) populations, ages 20-39 years and 70-89 years. Reprinted with permission from (5). Copyright 2007, The Endocrine Society. *NHANES* = National Health and Nutrition Examination Study; TSH = thyroid-stimulating hormone.

THEN the consideration turns to: does the patient have a form of "treatable" hyperthyroid disease? MANY patients don't have one of the three treatable forms of hyperthyroidism that ACTUALLY respond to methimazole: <u>Graves' Disease</u>, toxic multinodular goiter and solitary hyperactive nodule. (slide 23)

These each have different strategies for treatment (slide 15) before consideration of radioactive iodine or surgery. Thus, we have to look at the clinical documentation of the providers to see if they examined the eyes and the anterior neck and commented on their exam of the thyroid in their notes. Lack of this documentation would raise questions of the thoroughness of the exam and the training of the provider.



The whole category of disruptive thyroiditis (silent thyroiditis, subacute thyroiditis, or drug induced hyperthyroidism [like amiodarone]). ALL will **not** respond to treatment with methimazole. These all have suppressed I-131 uptake on thyroid uptake scans. Dr McDermott did cover these in his attached report as well (slide 16).

Don't forget that the most common form of suppressed TSH in the elderly is actually over-treatment of hypothyroidism. In patients on replacement therapy the goal of therapy is a TSH of 4-6. (slide 25)

Dr McDermott's entire presentation which is made easier to follow by listening to his description of each slide. Treatment of the Methimazole responsive conditions are on slides 13-14-15. The other group of NON-Methimazle responsive forms of hyperthyroidism are listed on slide 16 with the recommended treatments. He does mention use of radioactive iodine scans to differentiate these different types of hyperthyroidism to see which type the patient has and thus determine who would qualify for use of methimazole (disruptive thyroiditis with low I-131 update doesn't benefit). He also mentioned Thyrotropin Receptor Antibody testing (TRAb) to confirm Grave's Disease if positive.

## In summary,

- When reviewing TSH labs pay attention to TSH values less than 0.45 for possible subclinical hyperthyroidism. THEN exam the eyes for changes suggestive of Graves' Disease, the neck for the size, potential tenderness and possible nodules in the thyroid and document these findings in your clinical notes.
- Obtain the Free T-4 and Total T3 (used to confirm that this is not OVERT hyperthyroidism and to plan the dosing of methimazole if appropriate). Do this BEFORE starting methimazole.
- Document your thinking of how you will differentiate the types of hyperthyroidism that this patient might have if the TSH was < 0.45. This documentation is needed to show that you have a patient who will even respond to methimazole (remember that the thyroiditis group with suppressed I-131 uptake don't respond).
- Once you have shown that the TSH is < 0.45 and that you think they may have one of the three types of subclinical hyperthyroidism that may respond to Methimazole, then put into your note your plan of further evaluation and treatment: obtain imaging or not (demented patients are very hard to image), obtaining TRAb testing and whether you plan to get an endocrine consultation if unsure of the diagnosis since only Graves, toxic multinodular goiter and toxic solitary nodules will respond to Methimazole. It was not discussed if portable US of the neck is a viable substitute for RAI 131 scans and uptake. The US may show the overall size of the gland and if nodules are present, but these are often highly user dependent and if the patient is uncooperative then it will be of little value. It also doesn't tell you which patients would have suppressed I 131 uptake by the gland (the disruptive thyroiditis group and Amiodarone (which would be on the med list).</p>
- Do not treat patients with TSH greater than 0.45 with Methimazole.
- <u>Do not treat patients with Methimazole if their form of thyroid disorder is one of the disruptive thyroiditis</u> forms or drug induced such as Amiodarone.
- When in doubt reach out to an Endocrinologist. Your local hospitals will have a list of Endocrinologists on their staff.

We thank Dr McDermott for sharing his knowledge. He is the President-elect of the American Thyroid Association and we were very fortunate to see and listen to his presentation. His presentation audio is on the CMDA website: <u>https://cmda.us</u> opens a link on the CMDA website - (you may have to right-click it and chose open link or something similar depending on your operating system) <u>Audio</u> You may need to fast forward toward the middle (<u>19 minutes and</u> <u>30 seconds</u> is the start of his talk) of the audio file to find the presentation by Dr McDermott. Here is the video link: <u>December 6 2022 CMDA Meeting</u> forward to <u>20 minutes and 20 seconds</u> to see and hear Dr McDermott's presentation.

Thank you again for your work in our Long-Term Care communities.

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